REMARKS

Claims 1, 3, 5-11, 13-16, 36-51, and 60-61 are pending. Claims 3, 5-11, 45-48, and 50-51 are withdrawn as they are directed to a non-elected species. As compared to the disposition of claims noted on the first page of the Office action, applicants note that claim 4 was cancelled in the last amendment.

35 U.S.C. § 112

Reconsideration is requested of the rejection of claim 1, 13-15, 36-44, 60, and 61 as not satisfying the enablement requirement of 35 U.S.C. § 112, first paragraph. Claim 1 is directed to a method of removing sodium from an animal patient suffering from hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload by administering specific cation exchange polymers. The Office asserts that the specification "while being enabling for administering an acid resin [to] rats with compromised kidney function, does not reasonably provide a basis for identification of an effective amount, for a given species, age, sex" of the animal suffering from the claimed diseases.[1] The Office further asserts that there are no results for the human studies and applicants presume beneficial results will be achieved for the claimed conditions, but extensive experimentation would be needed to determine if such results could be obtained.[2]

Applicants submit that the specification contains support sufficient to enable those skilled in the art to practice the inventions of claims 1, 13-15, 36-44, 60, and 61 without undue experimentation. The pharmaceutically active polymers of these claims are described in detail throughout the specification, particularly on pages 14-24, and methods of preparing these polymers are described, for example, on pages 24-25, and exemplified in Example 2 on pages 30-34. The specification also sets forth in detail the claimed methods of treatment on pages 25-27. All of these descriptions are written in clear and concise language using terms that are well-known to skilled persons.

Moreover, the specification describes on pages 6-14 and 25-27, that the polymers of the present claims remove sodium from the body by binding and removing the sodium from the

[1] See Office action dated May 20, 2008 at page 2.
[2] See id.

gastrointestinal tract, that this sodium removal from the body affects the sodium concentration and water balance, and that the effect on sodium concentration and water balance has a beneficial effect for the claimed conditions. On pages 30 and 34-38, the specification details *in vitro* and *in vivo* tests to determine the activity of the pharmaceutical polymers. Further, the specification describes effective dosages and routes of administration on pages 27-30. These descriptions include the various modes by which the compounds can be administered to animals, the pharmaceutically acceptable forms in which they can be administered, and appropriate dosages for their administration. This information is sufficient to enable one skilled in the art to practice the inventions of the claims and accordingly, complies with the enablement requirement of 35 U.S.C. § 112.

A specification that contains a teaching of the manner and process of making and using the invention in terms that correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as an enabling disclosure unless there is reason to doubt the objective truth of the statements contained therein. As acknowledged in M.P.E.P. § 2164.04, the court in *In re Marzocchi* held that:

> "it is incumbent on the Patent Office whenever a rejection [for enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in the supporting disclosure and to back up such assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."[3]

In this case, the Examiner appears to be relying solely upon the breadth of the claims as a basis for doubting enablement. A rejection merely for breadth, however, is not appropriate, as explained in *In Re Borkowski*,[4] *In re Robins*,[5] and in *Marzocchi* itself. Here, except for asserting that a person of skill in the art cannot determine if the claimed conditions, doses, or benefits apply to animals or humans, the Office has not provided cogent reasoning to doubt applicants' specification. Thus, the Office has not met its burden of showing a *prima facie* case of lack of enablement under 35 U.S.C. § 112.

Applicants are not required to provide chemical or biological data as long as a description of each claimed invention is provided in clear and concise terms sufficient to enable a skilled person to practice each invention. Additionally, experimental examples are not required to

[3] *In re Marzocchi*, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).
[4] 164 U.S.P.Q. 642 (C.C.P.A. 1970).
[5] 166 U.S.P.Q. 552 (C.C.P.A. 1970).

support the complete scope of the claim. As stated in *In re Goffe*,[6] an applicant should not be required to limit the claims to materials disclosed in the examples because "[t]o demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts."[7]

Furthermore, and in any event, the experimentation required to test for the effective amount of a cation exchange polymer for each condition is not undue because a person of ordinary skill would know how to test for this using the guidance provided in the specification and such testing would be routine. Thus, claims 1, 13-15, 36-44, 60, and 61 satisfy the enablement requirement of 35 U.S.C. § 112.

35 U.S.C. § 103 Rejection

Reconsideration is requested of the rejection of claims 1, 13-15, 36-44, 60, and 61 as unpatentable under 35 U.S.C. § 103(a) over EP 0349453 (Martani) in view of U.S. Patent No. 5,846,990 (Murugesan) and Notenbomer (EP 0730494). Claim 1 is described above. The Office asserts that Martani provides disclosure of the claimed cation exchange moieties and administration of the Martani compositions would have removed sodium from a patient and that it would have been obvious that the Martani compositions combined with the Murugesan and Notenbomer drugs would have improved the status of a patient.[8]

There are three criteria for establishing a prima facie case of obviousness. First, there must be some reason either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in the way the claimed invention does. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Thus, the issue is whether it would have been obvious to treat the claimed conditions by administration of the specified sodium binding polymers. The U.S. Supreme Court in *KSR v. Teleflex* relied on predictability of the results as a basis for obviousness by stating that when a combination of known elements by known methods yields predictable results, the invention is

[6] 191 U.S.P.Q. 429, 431 (C.C.P.A. 1976).
[7] See id. at 431.
[8] See Office action dated May 20, 2008 at pages 3-4.

likely to be obvious.[9] However, the success of the treatment of the claimed conditions with a sodium binding polymer in an animal subject is unpredictable.

Further, as noted in M.P.E.P. §2112.IV, an obviousness rejection based upon the inherency of a claimed element must be supported by evidence that the missing element is necessarily present in the references, and that it would be so recognized by one skilled in the art:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). . . .
>
> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) (Applicant's invention was directed to a biaxially oriented, flexible dilation catheter balloon (a tube which expands upon inflation) used, for example, in clearing the blood vessels of heart patients). The examiner applied a U.S. patent to Schjeldahl which disclosed injection molding a tubular preform and then injecting air into the preform to expand it against a mold (blow molding). The reference did not directly state that the end product balloon was biaxially oriented. It did disclose that the balloon was "formed from a thin flexible inelastic, high tensile strength, biaxially oriented synthetic plastic material." *Id.* at 1462 (emphasis in original). The examiner argued that Schjeldahl's balloon was inherently biaxially oriented. The Board reversed on the basis that the examiner did not provide objective evidence or cogent technical reasoning to support the conclusion of inherency.).

Martani discloses compositions for the prolonged release of various cationic or anionic active ingredients. The cationic active ingredients are loaded on various anionic resins, particularly, polystyrene sulfonate resin and then the polystyrene sulfonate-active ingredient complex is coated with either an anionic (e.g., Eudragit® S) or preferably, a cationic (e.g.,

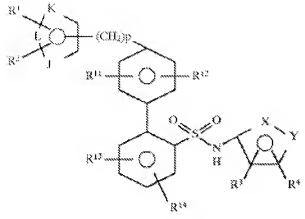
[9] See *KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727 (2007); 85 U.S.P.Q.2d 1385, 1395 (2007).

Eudragit® RL) polymer coating to delay the release of the active ingredient once administered. For anionic active ingredients, a cationic resin such as cholestyramine is used to complex the active ingredient and an anionic polymer coating (e.g., Eudragit® S) is used to coat the cholestyramine-active ingredient complex.

The specific cation exchange moieties specified by claim 1 and the *in vivo* sodium binding capacity of 4 mmol or more per gram of said polymer would not have been obvious from the Martani disclosure. Martani is concerned with controlled release of various active ingredients that are ionic. For this purpose, polystyrene sulfonate is exemplified, but Martani provides no disclosure that would have led a person of ordinary skill to select the particular cation exchange polymers required by claim 1 from the universe of possible cation exchange polymers. Moreover, the polystyrene sulfonate typically has an *in vivo* sodium binding capacity of about 1 meq/gram polymer[10] and there is no disclosure in Martani that would have led a person of ordinary skill to have expected that the Martani compositions would necessarily have an *in vivo* sodium binding capacity of at least 4 mmol/g as required by the claims. Further, Martani does not disclose or provide a reason to use the composition for treatment of a subject having any of the claimed conditions (e.g., hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload). Thus, the Martani disclosure would not have provided a skilled person with a reasonable expectation that the compositions would be useful to treat a subject having any of the claimed conditions or that the compositions would have had the sodium binding capacity required by claim 1.

Murugesan discloses various small molecule sulfonamide compounds having the following formula:

[10] See Emerson et al., "The role of the gastro-intestinal tract in the adaptation of the body to the prevention of sodium depletion by cation exchange resins" Ann N Y Acad Sci., 57(3):280-290 (1953).



These sulfonamides are described as endothelin antagonists useful to treat hypertension. While the Murugesan compounds are useful to treat hypertension, a person of skill in the art would not have had a reason to combine the disclosure of Murugesan with Martani because the small molecules of the Murugesan sulfonamides are absorbed and act as endothelin antagonists. Such small molecule receptor antagonists' mechanism of action is to block the endothelin receptor sites to inhibit the effects of endothelin, an effective vasoconstrictor. In contrast, the sodium-binding polymers of the claimed invention are not absorbed from the gastrointestinal tract and they bind and remove sodium from the animal's system. One of ordinary skill would have had no more reason to combine Murugesan with Martani than to combine any other reference describing a compound useful for treating hypertension with Martani. The cited references provide no reason to select the particular compound disclosed by Murugesan from the universe of hypertension drugs described in the prior art. Absent some reason to combine the disclosures of the cited references, no *prima facie* case of obviousness has been established.

Notenbomer generally discloses methods and particles for binding monovalent cations. The particles have a nucleus and a coating; the nucleus contains a cation exchange material and the coating comprises a membrane that is permeable for monovalent cations. This coating is disclosed as being more permeable for monovalent cations than for bi- or higher valent cations. Exemplified cation exchange materials are polyphosphate and polystyrene sulfonate resins and exemplified coatings are cellulose acetate and polyethyleneimine. The polystyrene sulfonate resin coated with crosslinked polyethyleneimine was shown to have an *in vitro* binding capacity for sodium of 1.4 mmol/g. These particles can be used to treat hypertension.

Notenbomer does not remedy the deficiencies of the Martani and Murugesan references. The Notenbomer compositions had an *in vitro* binding capacity of 1.4 mmol/g and would not have led a person of ordinary skill to suspect that these compositions would necessarily have an *in vivo* sodium binding capacity of at least 4 mmol/g as required by the claims. In fact, a skilled person could have expected that compositions having an *in vitro* binding capacity of 1.4 mmol/g in an ionic solution having a great majority of sodium ions would have an *in vivo* sodium binding capacity of even less than 1.4 mmol/g. Thus, the Notenbomer disclosure would not have provided a skilled person with a reasonable expectation that the compositions would have necessarily and inevitably had the sodium binding capacity required by claim 1. For at least the reasons detailed above, claims 1, 13-15, 36-44, 60, and 61 as patentable over EP 0349453 (Martani) in view of U.S. Patent No. 5,846,990 (Murugesan) and Notenbomer (EP 0730494) under 35 U.S.C. § 103(a).

Provisional Double Patenting Rejection

Reconsideration is requested of the provisional rejection of claims 1, 12, and 36-44 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 30, 31, 40, and 45 of copending Application No. 10/965,274 and the provisional rejection of claims 1, 12-14, 36-43, 60, 61 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 43-49, 52-59, and 61-64 of copending Application No. 11/096,209. It is noted that these rejections are provisional and upon issuance of patents, applicant will consider filing a terminal disclaimer to obviate this basis for rejection when the application is otherwise in condition for allowance.

Rejoinder

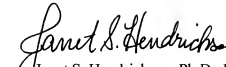
Pursuant to MPEP §821.04, Applicants again request rejoinder of withdrawn claims 3, 5-11, 45-48, and 50-51 as they depend from claim 1, require all of the limitations of claim 1, and claim 1 is amended to include specific acid resin polymers. Furthermore, applicants submit that these claims are allowable over the references relied upon by the Office.

CONCLUSION

Applicant submits that the present application is in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,



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